

Figure 1a. A general mixture synthesis with fluorous tags using a mixture of tagged compounds.

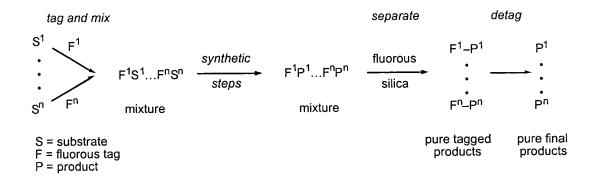


Figure 1b. A general mixture synthesis with fluorous tags using a mixture of tagged compounds and a mixture of reactants.

$$F^{1}S^{1}...F^{n}-S^{n} \xrightarrow{\text{react with}} F^{1}S^{1}R^{1}...F^{n}S^{n}R^{0} \xrightarrow{\text{separate}} \underbrace{\begin{array}{c} F^{1}S^{1}R^{1}...F^{1}S^{1}R^{0} \\ \vdots \\ F^{n}S^{n}R^{1}...F^{n}S^{n}R^{0} \\ \vdots \\ F^{n}S^{n}R^{1}...F^{n}S^{n}R^{0} \\ \end{array}}_{\text{each mixture comtains one S mixed with all R's}} \text{detagged products}$$

Figure 1c. A general mixture synthesis with fluorous tags using fluorous tagged reactants and a substrate.

$$S = \frac{\text{react with}}{R^1 F^1 - R^n F^n} = SR^1 F^1 \dots SR^n F^n = \frac{SR^1 F^1}{SR^n F^n} = \frac{SR^1 F^1}{$$

Figure 2. A representative example of a synthesis with a mixture of flourous tagged compounds and a mixture of reactants

3 libraries of 12 products, see below

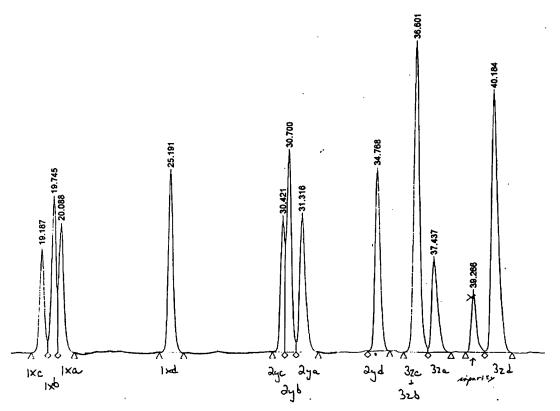
			Library	Esters	Products in order of retention times (min) on Fluofix column
Tags R <sup>f</sup>	Esters R <sup>1</sup> R <sup>2</sup>	Thiols	1	1x, 2y, 3z	1xc (18.5); 1xb (18.9); 1xa (19.3); 1xd (23.8); 2yc (28.7); 2yb (28.7); 2ya (29.5); 2yd (32.6); 3zc (34.1); 3zb (34.1); 3za (35.1); 3zd (37.9)
x C <sub>6</sub> F <sub>13</sub> y C <sub>8</sub> F <sub>17</sub> z C <sub>10</sub> F <sub>21</sub>	1 Me H 2 Pr H 3 H Me	a C <sub>6</sub> H <sub>5</sub> b 2-naphthyl c p-MeOC <sub>6</sub> H <sub>4</sub> d p- <sup>1</sup> BuC <sub>6</sub> H <sub>4</sub>	2	1y, 2z, 3x	3xc (18.1); 3xb (18.5); 3xa (18.7); 3xd (23.4); 1yc (27.0); 1yb (27.0); 1yc (27.6); 1yd (31.2); 2zc (35.6); 2zb (35.6); 2za (36.5); 2zd (38.8)
			3	1z, 2x, 3y	2xc (20.4); 2xb (20.9); 2xa (21.0); 2xd (25.3); 3yc (26.4); 3yb (26.4); 3ya (27.0); 3yd (30.8); 1zc (34.2); 1zb (34.2); 1za (35.1); 1zd (37.8)

APPROVED O.G. FIG.

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Figure 3. A representative HPLC trace of a library of compounds produced in the synthesis of Figure 2.<sup>a</sup>



a) Retention times are listed in minutes; compound numbers refer to Figure 2; Fluofix column eluting with a gradient of 80% methanol/water increased to 100% methanol over 40 min. The peak at 39 min is an unknown impurity.

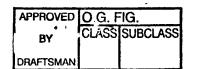


Figure 4. Preparation of Precursors for a Mixture Synthesis of Mappicine Analogs

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Figure 5. Mappicine Mixture Synthesis and Separation

Individual, pure samples of 6a,e

Mixture of 5a-e

separate on Fluofix™

Mixture of protected mappicines 6a-e

Retention Time Yield Time Gradient 36% 41% 29% 0-5 min 80% MeOH/H<sub>2</sub>O-3 min а 5-25 min 90% MeOH/H<sub>2</sub>O b 13 min 18 min >25 min 100% MeOH C ď 36% 21 min 28 min 43%

Figure 6. Preparation of precursors for a mixture synthesis of mappicine analogs (Example 8)

OMe

TMS

OMe

$$PrMgCI; R^3CHO$$
 $R^2 = Et, 87\%$ 
 $R^2 = CH_2Ph, 69\%$ 

OMe

OMe

OMe

OMe

 $R^2 = CH_2Ph, 69\%$ 

**4a** 
$$R^2 = CH_2Ph$$
,  $R^1 = {}^tBuMe_2Si$ , 79%  
**4b**  $R^2 = Et$ ,  $R^1 = H$ , 86%  
**4c**  $R^2 = {}^tBu$ ,  $R^1 = H$ , 68%  
**4d**  $R^2 = CH_2Ph$ ,  $R^1 = H$ , 62%

**4e** 
$$R^2 = Et$$
,  $R^1 = Ph$ , 69%